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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/442,143	11/15/99	LEVY G	9579-14

001059 HM12/0328
BERESKIN AND PARR
SCOTIA PLAZA
40 KING STREET WEST-SUITE 4000 BOX 401
TORONTO ON M5H 3Y2
CANADA AIR MAIL

EXAMINER	
CLEMENS,K	
ART UNIT	**PAPER NUMBER**
1644	8

DATE MAILED: 03/28/01
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/442,143	Applicant(s) LEVY ET AL.	
	Examiner Karen Clemens	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1,6-16 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. This application is continuation of PCT/CA98/00475 application, filed May 15, 1998 which claims priority to provisional application 60/061684 filed October 10, 1997 and provisional applications 60/046,537 filed May 15, 1997.

Applicant should amend the first line of the specification to include the status and relationship to the provisional priority documents.

2. Claims 1-21 are currently pending.

3. Applicant's election of Group III, Claims 2-5 and 17, drawn to a method of preventing or treating fetal loss by administration of an Fgl2 specific antibody, in Paper No. 7, dated 2/6/01 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

4. Claims 1, 6-16 and 18-21are withdrawn from further consideration by the Examiner as being drawn to nonelected inventions (see 37 C.F.R. 1.142(b)).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. 1.48(b) and by the fee required under 37 C.F.R. 1.17(h).

5. Claims 2-5 and 17 are currently under examination.

6. Drawings have been submitted which fail to comply with 37 C.F.R.1.84. Please see the enclosed form PTO-948.

7. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

8. Claims 4-5 and the specification are objected to under 37 CFR 1.821(d) because the said claims recite an amino acid sequence and do not recite a proper sequence identifier. Similarly, the specification (page 7, line 10 and Table 3, page 55, Figures 2-9 and 17, as well as the brief description of drawings, pages 4-5, for example) should include sequence identifiers adjacent referenced sequences. Applicants are required to include the appropriate SEQ ID NOs in the both the specification and the claims.

9. Claims 3-5 and 17 are objected to for being dependent upon nonelected claims 1 and 15, respectively. Applicant is required to amend claims 3-5 and 17 to reflect the limitations of non-elected claims 1 and 15.

10. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 2, 3 and 17 are rejected under 35 U.S.C.§ 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims 2, 3 and 17 are drawn to an *inhibitor* of Fgl2 or an *antibody that binds Fgl2*..

However, Applicant's disclosure is limited to *inhibitors* of Fgl2 which include antisense DNA specific for the polynucleotides of SEQ ID NO:1 and 3 and *antibodies* specifically directed against the polypeptide of SEQ ID NOs:2 and 4 and that recognize the epitope of amino acids sequences of 364-378 of SEQ ID NO:2 and 4.

The Applicant has not disclosed, nor does the art recognize, the claimed *genus* of *inhibitors* of Fgl2, including *any inhibitor* of Fgl2 other than the antisense DNA specific for the polynucleotides of SEQ ID NO:1 and 3 SEQ ID NO:2 or 4 and the *antibodies* to SEQ ID NO:2 and 4 or to epitopes in amino acids sequences of 364-378 of SEQ ID NO:2 and 4 in which there exists an established correlation or

relationship between the *structure* of the instant invention and its *function*, deemed essential to the instant invention. One skilled in the art would not envisage, from the instant disclosure, the aforementioned genus of *inhibitors* of Fgl2 or *antibodies to Fgl2* outside of the instant antisense nucleic acids to SEQ ID NO:1 and 3 and antibodies to SEQ ID NO:2 and 4 or to amino acids sequences of 364-378 of SEQ ID NO:2 and 4. Therefore, one of skill in the art would not recognize the Applicants to be in possession of the genus of *inhibitors* of Fgl2 or *antibodies that bind Fgl2* as claimed.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See *Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).* Applicant is also directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 2-5 and 17 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for preventing or treating fetal loss comprising administering an antibody to SEQ ID NO:2 or 4 does not reasonably provide enablement for use of *any antibody to Fgl2*, including any antibody which recognized an epitope to amino acids 364-378 of SEQ ID NO:2 and 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the unpredictability in the

art and amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. The specification discloses use of an Fgl2 antibody which is directed against SEQ ID NO:2 or 4 for use in treating or preventing fetal loss. However, the specification fails to provide guidance as to how to determine specifically which *other* antibodies, specifically antibodies which bind the epitope of amino acids 364-378 of SEQ ID NO:2 and 4, would function in treating or preventing fetal loss.

The current state of the art in epitope structure prediction is limited given that noncontiguous amino acid residues constitute most epitopes, and that the dynamics of binding is often not integrated into the epitope prediction equation, making epitope structure prediction a complex four-dimensional problem (see Van Regenmortel, page 465, abstract in particular; *Methods: A Companion to Methods of Enzymology* 9:465-472). Van Regenmortel notes that 90% of antibodies raised against intact proteins do not react with any peptide fragment derived from the parent protein indicating that these antibodies are directed to discontinuous epitopes (see page 466, column 1 in particular). In addition Van Regenmortel states that the low success rate of antigenic prediction is due to the fact that predictions concern only continuous epitopes and it is unrealistic to reduce the complexity of epitopes that always possess conformational features to one-dimensional, linear peptide models (see page 467, column 2 in particular). . Detailed information regarding the specific epitopes recognized by the instant antibodies to SEQ ID NO:2 and 4 and whether those antibodies would function in preventing or treating fetal loss is lacking. Therefore, predicting which antibodies outside of the antibodies to SEQ ID NO:2 or 4 in the prevention or treatment of fetal loss is well outside the realm of routine experimentation. A skilled artisan would require guidance, such as information regarding the specific epitope recognition of the antibodies successfully used in the instant invention in order to antibodies other than those directed against SEQ ID NO:2 and 4 in a manner reasonably commensurate with the scope of the claims. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention.

In view of the lack of sufficient guidance in the specification and a limited number of working examples, the unpredictability in the art and the breadth of the claims it would take an undue amount of experimentation for one skilled in the art to practice the invention as claimed.

12. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> "The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention."

Claims 2-5 and 17 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 5 is indefinite and ambiguous in the recitation of "amino acids at positions 364-378....in Figure 5" since two polypeptides, mouse and human Fgl2, polypeptide are disclosed and differ in length, making the exact identification of amino acid positions 364-378 unclear.

Claim 17 recites a "composition" but only a *compound* comprising an antibody specific for an Fgl2 protein is recited in non-elected claim 15 (and the non-elected species of anti-sense DNA). The claim as written reads on compounds not compositions.

Claims 2-5 and 17 are indefinite and ambiguous in the recitation of a "method of ...treating a fetal loss". It is unclear how one would "treat" a fetal loss, other than to prevent or reduce the risk of fetal loss.

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Clemens whose telephone number is (703) 308-8365. The examiner can normally be reached Monday through Friday from 8:00 AM to 5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in

Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Karen Clemens, Ph.D.
Patent Examiner
Technology Center 1600
March 23, 2001

Christina Chan

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640